REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. §1.112, are respectfully requested in light of the remarks that follow.

Upon entry of the foregoing amendment, Claims 22-92 will be in the application.

The foregoing amendment to the specification is intended to update the cross-reference to Companion Application in the application text as filed. The companion application is also discussed below.

Each of new Claims 22-84 is drawn to a regime/regimen for influencing calcium channels in muscle fiber to relax and/or slacken cutaneous and/or subcutaneous tissue, or skin tissue, comprising administering a particular cosmetic/dermatological composition. The claims have thus been rewritten to better reflect the mechanism by which the present invention operates to relax or slacken cutaneous and/or subcutaneous tissue, as in original Claim 15 and as discussed in paragraphs [0005] to [0020] of the specification.

In the broadest new claim, Claim 22, the composition administered comprises an amount of manganese and/or at least one salt thereof effective to influence calcium channels in muscle fiber to relax and/or slacken cutaneous and/or subcutaneous tissue, and a physiologically acceptable vehicle, diluent or carrier thereof; this claim replaces original Claim 1 as well as original Claim 6.

Claim 23 specifies that the composition of Claim 22 consists essentially of those ingredients.

Claim 24 specifies that the regime/regimen is for influencing calcium channels in muscle fiber to relax and/or slacken skin tissue and thus treat wrinkles and fine lines in the skin, that the administration is topical and that the manganese and/or at least one salt thereof is the only active ingredient for treating wrinkles and fine lines in the composition; this claim replaces original Claim 2.

Claim 25 depends from Claim 24, but specifies reducing wrinkles and fine lines, as in original Claim 3. This claim also replaces original Claim 16.

Claim 26 depends from Claim 22, but specifies that the method thus smooths the skin, as in original Claim 4; Claim 26 further specifies that the administration is topical and that the manganese and/or salt thereof is the only active ingredient for smoothing the skin in the composition.

Claim 27 also depends from Claim 22 but specifies that the method thus attenuates and/or eliminates microrelief in the skin, as in original Claim 5; Claim 27 further specifies that the administration is topical and that the manganese and/or salt thereof is the only active ingredient for attenuating and/or eliminating microrelief in the skin in the composition.

Claim 28 is an independent claim which replaces original Claim 7 and contains language paralleling that found in Claims 25, 26 and 27 as discussed above.

Claim 29 is an independent claim which parallels Claim 28 but uses "consisting essentially of" language and specifies the presence of (ii) a bioaffecting amount of alverine or salt thereof, a keratolytic agent, a chlorine-channel opener, a hydroxy acid and/or a retinoid. This claim replaces original Claim 20.

Claim 30 depends from Claim 29, but limits (ii) to a bioaffecting amount of alverine or salt thereof and/or a chlorine-channel opener. This claim does not correspond to an original claim but is of course supported by at least original Claim 20.

Claims 31 and 33 parallels Claims 22 and 24, respectively, but further specify that from 0.0001% to 10% by weight of manganese is administered; this is supported by at least original Claim 8.

Claims 32 and 34 also parallel Claims 22 and 24, respectively, but specify that the manganese is administered as at least one inorganic and/or organic manganese salt; this is supported by at least original Claim 11.

Claim 35 parallels Claim 22, but further specifies that manganese is administered as at least one of the organic salts named in original Claim 12.

Claim 36, which depends from Claim 35, is based on at least Examples 2, 4 and 5.

Claim 37 parallels Claim 27, but further specifies that manganese is administered as at least one of the inorganic salts named in original Claim 13.

Claim 38, which depends from Claim 37, is based on at least Example 3.

Claims 39, 40 and 43-48 further limit Claims 22, 23, 31, 32 and 35-38, respectively, to topical administration, the preferred route of administration specified, for example, in original Claim 16.

Claims 41 and 42 specify administration orally or by injection as in original Claims 17 and 18, respectively.

Claims 49, 50 and 51 depend directly or indirectly from Claim 22 and find support at least in original Claims 9, 10 and 19, respectively.

Claims 52-58 depend directly or indirectly from Claim 23 and specify features set forth in original Claims 8-13 and 19, respectively.

Claims 59-63 depend directly or indirectly from Claim 24 and specify features set forth in original Claims 9, 10, 12, 13 and 19, respectively.

Claims 64-70 depend directly or indirectly from Claim 28 and specify the features set forth in Claims 8-13 and 19, respectively.

Claims 71-77 similarly depend directly or indirectly from Claim 29 and specify the features set forth in Claims 8-13 and 19, respectively.

Claims 78-84 similarly depend directly or indirectly from Claim 30 and specify the features set forth in Claims 8-13 and 19, respectively.

Claim 85 is the only independent composition claim in the application and thus replaces original Claim 21. However, Claim 85 uses "consisting essentially of" language and ingredient (ii) therein is a bioaffecting amount of alverine or salt thereof and/or a chlorine-channel opener. Claims 86-92 depend from Claim 85 and specify features set forth in original Claims 8-13 and 19, respectively.

It is clear from the foregoing that the amendments set forth above do not introduce new matter into the application.

We turn now to the Official Action.

All of applicants' claims have been provisionally rejected as unpatentable over Claims 1-15 of copending Application No. 09/859,392. Copending Appln. No. 09/859,392 was filed concurrently herewith, and has not yet been allowed. Applicants submit that it would be appropriate to first allow one of the applications and then to

consider whether the claims of the non-allowed application should be rejected for obviousness-type double patenting over the allowed claims of the other application. At the present time, it is agreed that the two applications contain overlapping composition claims and that it would be appropriate to file a terminal disclaimer in either this or the copending application, if this overlap continues when one of the applications has been allowed. With respect to the method claims, however, the methods in the two applications are clearly distinct, since the method claims of the '392 application at the present time are drawn-to methods of combating skin pallor in an individual subject in need of such treatment, while the instant method claims are drawn to a regime/regimen for influencing calcium channels in muscle fiber to relax and/or slacken cutaneous and/or subcutaneous tissue in an individual subject in need of such treatment. In the present case, the claimed method affords a means of treating/diminishing wrinkles and fine lines, of smoothing the skin or of attenuating and/or eliminating microrelief in the skin; in the '392 application, the method is applied to a very different subject, one who needs the restoration of natural color to a skin gone pale from stress. Thus, the method claims are not believed to overlap at the present time.

Many of applicants' claims have been rejected under 35 U.S.C. §112, first paragraph, because the specification is said to provide sufficient enablement for reducing wrinkles but not for preventing them. This rejection has been rendered moot by the wording of the new claims, which do not contain any form of the word "prevent". Nevertheless, it is submitted that it was never applicants' intention to claim that the subject never experiences any characteristics associated with wrinkles, and that the Examiner

interprets the term "prevent" too strictly and not in the manner in which it would be understood by one of ordinary skill in the art. At any rate, the word in question does not appear in the new claims and the rejection should therefore be withdrawn.

Many of applicants' claims have also been rejected because of the use of certain terms in the original claims. Each of the criticized expressions is discussed below.

(i) The terms "slackening" and "relaxing" are used in the new claims as well. These terms are believed to be the appropriate ones to use in the context of the invention, and are in accord with the usual dictionary meaning of loosening or reducing the tautness of. The instant description makes clear that contractile elements in facial skin, i.e. myofibroblasts in dermal tissue and muscle fibers in the hypoderm [0006] serve an essential function in the formation of wrinkles and that cutaneous and subcutaneous tissue comprise calcium channels [0019]. As the muscle contraction/relaxation phenomenon is mediated by variation of intracellular calcium [0014], applicants show that the use of manganese promotes the relaxation of contractile fibers and so relaxes and/or slackens cutaneous and/or subcutaneous tissue. The claim language is thus quite clear and the rejection based on this terminology should be withdrawn.

(ii) The expression "curatively" was originally used to distinguish from "preventively" treating wrinkles. The corresponding claims now simply refer to "treating" wrinkles, making this rejection moot.

(iii) The term "thus-effective" was originally sued to succinctly express what the amount was effective for. The claims now spell out the purpose, so that the term "thus-effective" is no longer needed. This rejection is thus moot as well.

(iv) The expression "muscularly relaxing" of course was clear from paragraphs [0014] to [0020] of the specification. Somewhat different wording is used in the new claims to better convey the fact that the relaxing and/or slackening of cutaneous and/or subcutaneous tissue results from modulation of the contraction of muscle fibers. This rejection has thus also been rendered moot.

(v) The term "microrelief" is well-known and understood in the cosmetic art and is appropriately used in applicants' claims. Microrelief refers to the micro-depressions on the surface of the skin, i.e. fine lines and wrinkles, generated by fiber contraction phenomena. Applicants request withdrawal of the rejection based on this terminology.

(vi) The term "manganese-rich" is explained in the specification in paragraphs [0050] and [0051]. This is a natural, plant or microorganism extract obtained from a material naturally rich in manganese (such as nut or tea) and extracted so that the extract contains manganese in the appropriate amount (i.e. to provide 0.0001% to 10% manganese by weight of the total weight of the composition).

(vii) Applicants apologize for the grammatical error in Claim 19. The new claims are believed to be free of this rejection, which is moot. With respect to the Examiner's question, the answer is no. All of these preparations are topically applicable, but they are typically suspensions rather than solutions.

In view of the foregoing, it is submitted that the new claims are free of all record 35 U.S.C. §112 rejections.

Claims 1-7, 15, 20 and 21 have been rejected under 35 U.S.C. §102(b) as anticipated by Thorel (FR 2612775). It is believed that all of the claims now in the application are free of this rejection.

FR 2612775 (Thorel) is discussed in detail on pages 2-3 of the accompanying Information Disclosure Statement. All of applicants' method claims, i.e. Claims 22-84, are now drawn to a regime/regimen for influencing calcium channels in muscle fiber to relax and or slacken cutaneous and/or subcutaneous, or skin tissue, which is in no way suggested by Thorel, as apparently already recognized by the Examiner because she has not applied this rejection to Claim 16, drawn to such a regime or regimen. Likewise, Thorel does not disclose or suggest the use of manganese *per se* and/or a manganese salt *per se*, much less particular weights thereof, as specified in many of applicants' claims. Moreover, Thorel requires the presence of ascorbic acid as well as a plurality of vegetal extracts to provide sources of sulfur, manganese and magnesium. Applicants' method claims which specify that the composition administered consists essentially of manganese and/or at least one salt thereof and a physiologically acceptable vehicle, diluent or carrier (for example, Claim 23) or that the manganese and/or at least one salt thereof is the only active ingredient for treating wrinkles and fine lines in the composition (for example, Claim 24) are particularly remote from the Thorel reference. Moreover, applicants' composition claims are very narrow; the broadest composition claim now in the application uses "consisting essentially of" language and moreover requires a second ingredient (ii) which is a bioaffecting amount of alverine or salt thereof and/or a chlorine-channel opener. There is no disclosure or

suggestion of such a composition in Thorel. Thus, none of the present claims is believed to be anticipated by Thorel.

Claims 1-11, 13-16 and 19 have been rejected under 35 U.S.C. §102(b) as anticipated by EP 0424033 (Okaya et al). It is submitted that this rejection cannot be maintained against the claims now in this application.

It is noted that the Okaya et al document is not cited against applicants' composition claims. Since the amended composition claims are even narrower than the original ones, it is understood that this reference would not be applied to them either.

Okaya et al teach a method of stabilizing Mn-SOD and/or modified Mn-SOD in aqueous systems and an aqueous external skin preparation which contains, as essential components, manganese-containing superoxide dismutase and/or a polyalkylene glycol- or polysaccharide-bound modification of manganese-containing superoxide dismutase and a physiologically acceptable water-soluble manganese salt (page 3, lines 1-7 of Okaya et al). Okaya et al, beginning on page 2, line 50, explain that they wanted to provide an external skin preparation containing Mn-SOD and/or modified Mn-SOD, which would maintain the stability of the enzyme activity and thus have improved reducing potential against skin-roughening. They had already noted earlier on page 2, at lines 24-25, that Mn-SOD suffers from the fact that its enzyme activity decreases in aqueous systems, i.e., its stability in aqueous systems is unsatisfactory, which in turn limits its use in scavenging active oxygen. Okaya et al indicate on pages 2-3 that their preparation has improved reducing potential against skin-roughening by maintaining enzyme activity at a stable level; to arrive at this, Okaya et al considered that the decrease in enzyme activity of Mn-SOD and/or

modified Mn-SOD in aqueous systems was related to manganese atom elimination from the Mn-SOD/modified Mn-SOD. They found that they could stabilize Mn-SOD/modified Mn-SOD by adding a water-soluble manganese salt to the aqueous system. It is apparent from this discussion in the patent that the manganese salt added to the aqueous system containing Mn-SOD/modified Mn-SOD is simply replacing Mn ions which have been eliminated from the Mn-SOD in the aqueous system so that the Mn-SOD can be stable and can be utilized for its intended purpose; the Mn ions in the salt are not available for another purpose because they are simply replacing what has been eliminated from the Mn-SOD so that the Mn-SOD can be stabilized and can perform its intended function. The stabilizing effect of manganese chloride on Mn-SOD and on PEG-Mn-SOD is shown in Table 2 of the European patent; pages 4-5 of the patent show much better Mn-SOD enzyme activity when manganese chloride is present. Also, Table 3 of the patent (pages 5-6) shows that a composition containing modified Mn-SOD + manganese chloride was much superior to a composition containing only manganese chloride in skin roughening reducing effect. On page 6, at lines 14-16, Okaya et al conclude:

> As is evident from the foregoing description, the external preparation according to the invention is a very excellent one, showing good stability with a high residual enzyme activity percentage and further showing an antagonizing effect on the skin roughening otherwise caused by Mn-SOD. (Emphasis added).

Thus, applicants submit that the Okaya et al patent, taken in its entirety, clearly shows that the only role of the manganese salt therein is in replacing Mn ions in Mn-SOD/modified Mn-SOD so that Mn-SOD can perform its intended function. Because the

manganese salt is being used to replace Mn in Mn-SOD, so that Mn-SOD will work, the salt clearly is not available to act in some other respect.

Moreover, all of applicants' method claims are now drawn to a regime/regimen for influencing calcium channels in muscle fiber to relax and/or slacken cutaneous and/or subcutaneous tissue, or skin tissue, and now require that manganese and/or its salt be administered in an amount effective to influence calcium channels in muscle fiber to relax and/or slacken cutaneous and/or subcutaneous tissue, or skin tissue, in an individual subject in need of such treatment. Okaya et al teach nothing about influencing calcium channels in muscle fiber. There is no evidence on this record that Okaya et al's method can influence calcium channels in muscle fiber to relax and/or slacken cutaneous and/or subcutaneous tissue, or skin tissue. Still further, it is quite apparent here that one of ordinary skill, wanting to find a way to influence calcium channels in muscle fiber to relax and/or slacken cutaneous and/or subcutaneous tissue in a subject in need of such treatment, would find nothing in Okaya et al that would give that skilled worker a reason to use Okaya et al's composition to treat such a subject. Moreover, applicants' claims which use "consisting essentially of" language or which specify that manganese and/or its salt is the only active ingredient for treating wrinkles and fine lines (or similar terminology) in the composition administered clearly exclude a further active ingredient such as Mn-SOD or modified Mn-SOD from the composition administered and are clearly neither disclosed nor suggested by Okaya et al. Likewise clearly distinct are applicants' claims in which the composition administered contains the specific active ingredients enumerated therein, none of which is or includes Mn-SOD/modified Mn-SOD.

In view of the foregoing, the new claims are believed to be free of the §102(b) rejection based on Okaya et al.

Claims 1-17 and 19-21 have also been rejected under 35 U.S.C. §102(b) as anticipated by Hahn et al WO 96/19182. This rejection also cannot be maintained against the claims now in the application.

Hahn et al teach compositions and methods for reducing skin irritation attributable to chemical irritants or environmental conditions. Their compositions comprise a topical vehicle, an irritant and an anti-irritant amount of aqueous-soluble divalent magnesium cation, divalent manganese cation or trivalent cations of atomic numbers 57-71. Applicants' method claims are not directed to a method of reducing irritation, but rather to a method for influencing calcium channels in muscle fiber to relax and/or slacken cutaneous or subcutaneous tissue. Applicants' method is applied to an individual subject in need of this particular treatment, for example, a person suffering from wrinkles or fine lines in the skin, not to a person whose skin is irritated by a chemical irritant or an irritating environmental factor. One of ordinary skill is taught nothing by the Hahn et al method which would lead them to applicants' method which is for influencing calcium channels in muscle fiber to relax and/or slacken cutaneous or subcutaneous tissue and has nothing to do with irritation caused by chemical or environmental irritants. As to applicants' composition claims, such claims all use "consisting essentially of" language and require the presence of alverine or salt thereof and/or a chlorine channel opener, which are unsuggested by Hahn et al. Alpha-hydroxy acids and retinoids, disclosed as irritants by

Hahn et al, are no longer possible additional ingredients of the instant composition claims. Thus, all of applicant's claims are believed to be free of this rejection.

Claims 1-7, 10-11, 14-16 and 19 have been rejected under 35 U.S.C. §102(b) as anticipated by Sanders et al United States Patent No. 5,895,642. Once again, applicants submit that the present claims are free of this record rejection.

This rejection has not been applied to the original composition claim and, since the new composition claims are narrower than the original ones, we assume it is not relevant to them either. As to the new claims drawn to the method, the method of Sanders et al is a method of pigmenting skin depigmented by a tyrosinase-positive depigmentation disorder comprising applying to at least the depigmented areas of the skin an effective amount of a composition comprising a complex of ions of a transition metal, bicarbonate ions and a chelating agent for chelating the transition metal and for increasing pseudocatolase activity, and thereafter exposing the treated skin to UVB light to induce melanin formation. This is for treating conditions such as vitiligo (col. 1, lines 1-5, 25-27 and 45-56; Claims 1 and 19). Sanders et al also provide a method for enhancing tanning by applying the same composition. The metal can be manganese, iron or copper, and the specified chelating agent disclosed is EDTA. The invention of Sanders et al absolutely requires a chelating agent such as EDTA in the composition. Further, the method of Sanders et al is totally different from that of applicants, because the Sanders et al method relates to increasing melanin and would be applied to a person suffering from a vitiligo or other depigmenting disorder or a person desiring enhanced tanning of the skin. Applicants' method is for influencing calcium channels in muscle fiber to relax and/or slacken cutaneous or

subcutaneous tissue and would be applied to a person in need of such treatment, for example, a person suffering from wrinkles and fine lines in the skin; this has nothing to do with inducing melanin formation, the point of the method of Sanders et al. One of ordinary skill is taught nothing by the Sanders et al method which would lead them to applicants' method. All of applicants' claims are thus believed to be free of this rejection.

Claims 1-11, 13-16, and 19-21 have been rejected under 35 U.S.C. §102(b) as anticipated by Breton et al U.S. Patent No. 5,900,257. It is believed that this rejection cannot be maintained against the claims now in this application.

Breton et al describe a method for treating sensitive skin or a variety of cutaneous disorders in which there is an excess in the synthesis and/or in the release of substance P, comprising applying an effective substance P antagonist amount of at least one salt of one or more of eighteen metals, one of which is manganese. The method of Breton et al is substantially different from applicants' method. Breton et al's method is applied, typically by topical administration, to a person having sensitive skin or having a cutaneous disorder in which there is excess synthesis/release of substance P. The person to which Breton's substance P antagonist is applied is not the same as the person to whom applicants' method is applied. As noted above, applicants' method is for influencing calcium channels in muscle fiber to relax and/or slacken cutaneous or subcutaneous tissue and would be applied to a person in need of such treatment, for example a person suffering from wrinkles and fine lines in the skin. This has nothing to do with excess synthesis or release of substance P and thus one of ordinary skill is taught nothing by the Sanders et al method which would lead them to applicants' methods. As to applicants' composition claims, these use

"consisting essentially of" language and require the presence of (ii) a bioaffecting amount of alverine or salt thereof and/or a chlorine-channel opener. Breton et al teach that a number of active agents can be added to their compositions, but neither describe nor suggest alverine or a salt of alverine and/or a chlorine-channel opener. Thus, all of applicants' claims are believed to be free of this rejection.

Claims 1-7, 10-11, 15, 17 and 20-21 have been rejected under 35 U.S.C. §102(e) as anticipated by Riley et al U.S. Patent No. 5,925,348. The amended claims are believed to be free of this rejection.

Riley et al teach the use of an extract of the Sacred Lotus seed as an anti-aging agent in a cosmetic, dermatological and/or dietary composition and methods for treatment of aging using such compositions. One of the components of the Sacred Lotus plant, namely methyltransferase, is identified as being able to repair proteins which make up cells and tissues, thus slowing tissue decay. The patent clearly identifies Sacred Lotus plant extract or methyltransferase as responsible for repairing damaged skin and restoring skin to a more youthful appearance. The Examiner cites a dietary supplement in this patent as containing magnesium stearate, apparently formulated as a tablet for oral administration, but the present invention has nothing to do with magnesium. It is noted that the same formulation contains manganese gluconate, which is presumably what the Examiner intended to cite. The dietary supplement contains quite a variety of materials often found in vitamin/mineral dietary supplements, including manganese. There is no suggestion that manganese could treat wrinkles by any route of administration whatsoever or is essential to

Riley et al's invention. Indeed, Riley et al teach Sacred Lotus extract/methyltransferase as the active ingredient for treating aging skin.

As noted above, all of applicants' method claims are now drawn to a regime/regimen for influencing calcium channels in muscle fiber to relax and/or slacken cutaneous or subcutaneous tissue, or skin tissue; it is noted that this is a totally different method of treatment; moreover, this language appeared in original Claim 16, which has not been rejected based on Riley et al. It appears that the Examiner has already realized that Riley et al's treatment of wrinkles works by an entirely different mechanism than applicants' method; that mechanism is now specified in all of applicants' method claims. Note, too, that applicants' claims which specifically mention wrinkles use "consisting essentially of" language or specify that the manganese and/or manganese salt is the only active ingredient for treating such a condition, thus clearly excluding Sacred Lotus plant extract/methyl transferase. As to applicants' composition claims, these use "consisting essentially of" language and require the presence of alverine, an alverine salt or a chlorine-channel opener, thus excluding Riley et al's essential Sacred Lotus plant extract/methyl transferase and requiring ingredients found in none of Riley et al's compositions. Clearly, this reference cannot be maintained against the instant claims.

Claims 1-7, 10, 14 and 19 have been rejected under 35 U.S.C. §102(b) as anticipated by Kaneko JP 09157128 (abstract only). The claims now in the application are free of this rejection.

Initially, it is noted that the Kaneko reference has not been cited against applicants' composition claims. As to applicants' method claims, it is again noted that all of the

method claims now recite the mechanism of action recited in original Claim 16, which was not subject to this rejection.

Kaneko is directed to aging prevention by maintaining and promoting healthy normal flora of the skin by using in a cosmetic a minute amount of manganese, zinc or their salts. Kaneko thus focuses on the barrier function of the skin. All of applicants' method claims are now directed to a regime/regimen for influencing calcium channels in muscle fiber to relax and/or slacken cutaneous or subcutaneous tissue, or skin tissue, which is completely unrelated to maintaining or promoting healthy normal flora of the skin. Thus, this rejection too should be withdrawn.

Claims 7 and 18 have been rejected under 35 U.S.C. §103(a) as unpatentable over Hahn et al. This rejection is limited to method claims and cannot be maintained against the method claims now in this application.

Hahn et al is fully discussed above and relates to reducing skin irritation, not to influencing calcium channels in muscle fiber to relax and/or slacken cutaneous or subcutaneous tissue as specified in all of applicants' claims. The fact that Hahn et al contemplate use of a manganese cation to reduce irritation caused by a irritant teaches nothing to the ordinary skilled worker which would motivate him toward, or for him to have a reasonable expectation of success in, using manganese to influence calcium channels in muscle fiber to relax and/or slacken skin tissue and to, for example, thus treat wrinkles. The methods clearly are distinct and involve completely different mechanisms. This rejection should not be maintained against any of the claims now in the application.

Claims 7, 10, 11, 12, 17 and 18 have been rejected under 35 U.S.C. §103(a) as unpatentable over Breton et al. We submit that all of the claims now in the application are free of this rejection. It is noted that this rejection is only applied to method claims.

Breton et al is fully discussed above. Breton et al teach the use of a manganese salt as a substance P antagonist to treat sensitive skin and disorders associated with excessive synthesis or release of substance P. All of applicants' method claims are now drawn to a method of influencing calcium channels in muscle fiber to relax and/or slacken cutaneous or subcutaneous tissue; there is no suggestion in Breton et al of such a use of manganese. On the contrary, Breton et al focus on treating disorders associated with excess substance P, especially sensitive skin. Even if Breton et al would have suggested the use of a composition with applicants' specific Mn salts and/or formulated for oral or injectable administration, it would have been for Breton et al's purposes. Breton et al does not suggest that his compositions could be used to influence calcium channels in muscle fiber to relax and/or slacken cutaneous tissue. This specific application was not disclosed or even suggested by the prior art. Again, the record rejection should not be maintained against the present claims.

As to the Examiner's comments regarding unexpected results, we submit that since the subject matter now claimed is not obvious from the art, as clearly pointed out above, there is no burden on applicants to demonstrate unexpected results. But, indeed, the very fact that manganese can be used to influence calcium channels in muscle fiber to relax or slacken cutaneous or subcutaneous tissue as reflected in the instant claims is quite

surprising in light of the prior art. The art contains not a scintilla of a suggestion of applicants' invention.

It is also submitted that the 35 U.S.C.§102 rejections of applicants' method of use claims are particularly ill-founded and ignore the essential differences in determining the patentability of method of use claims versus composition claims.

The Court of Appeals, Federal Circuit and its predecessor, the Court of Customs and Patent Appeals, have repeatedly held that anticipation requires that all elements and limitations of the claim must be found within a single prior art reference. There must be no difference between the invention claimed and the disclosure of the reference as viewed by one of ordinary skill in the art; Scripps Clinic Research Foundation v. Genetech Inc., 18 U.S.P.Q.2d 1001; In re Marshall, 198 U.S.P.Q. 344. Anticipation can nevertheless be made out if the invention is inherently disclosed in the art, that is, if one of ordinary skill in the art would reasonably expect the claimed invention from the disclosure of the reference; conversely, however, if the disclosure of the reference, coupled with the knowledge of the ordinary skilled worker, does not lead one of ordinary skill to reasonably expect the claimed invention, there can be no anticipation.

Applicants' utility is not disclosed by the references. The Examiner must therefore make out a case of inherency in order to support her §102 rejections of the method claims. However, in relying on inherency, the Examiner is required to provide a basis in fact or technical reasoning to show that the present invention necessarily flows from the references' teachings; see, for example, Ex parte Levy, 17 U.S.P.Q.2d 1461. This the Examiner has not done and, indeed, this she cannot do. It is not immaterial whether

manganese or its salts was/were known to possess utility in influencing calcium channels in muscle fiber to relax or slacken cutaneous or subcutaneous tissue. This utility was not known, nor would it have been reasonably expected by the ordinary skilled worker reading any of the cited prior art disclosures, as it does not necessarily flow from the properties disclosed in the art. Applicants believe it is highly surprising that they have found that manganese or its salts is/are useful for the purpose here disclosed. Moreover, although the manganese salt may be applied to a subject by the same route of administrative herein as in the references, the method being practiced is entirely different. The claim language makes this clear.

It is believed that the C.C.P.A. decision in In re Marshall, 198 U.S.P.Q. 344, is very much in point here insofar as concerns the Court's reversal therein of the Board of Appeals' decision sustaining the Examiner's 35 U.S.C. §102 rejection of Claims 1-4. Appellants' invention as claimed in Claims 1-4 was a weight control process in which an effective amount of oxethazaine was administered to inhibit release of the pancreatic secretory hormones so as to control weight. The rejection of these claims was reversed because the primary reference, the PDR (*Physician's Desk Reference*), did not disclose every material element of the claimed subject matter. The Court said that the PDR taught use of oxethazaine to inhibit release of the acid-stimulating hormone, gastrin, to treat certain digestive disorders; but that the PDR did not remotely suggest taking oxethazaine to lose weight. The rejection of Claims 1-4 was therefore reversed. Whether or not the dosages for the two uses overlapped played no role in the decision in the §102 rejection; the key holding was that the reference did not disclose using the drug to lose weight. The

Court also stated: "If anyone ever lost weight following the PDR's teaching, it was an unrecognized accident. An accidental or unwitting duplication of an invention cannot constitute an anticipation." Similarly, in the present case, the references do not anticipate applicants' claims because the references do not disclose or even remotely suggest applying a manganese salt to influence calcium channels in muscle fiber to relax and or slacken cutaneous or subcutaneous tissue.

Further, in connection with the obviousness rejections, the C.C.P.A.'s decision in In re Shetty, 195 U.S.P.Q. 753, is believed to be enlightening. In that case, the Court specifically cautioned against the sort of reasoning the Examiner has used here in assessing the patentability of method of use claims. Shetty claimed compositions comprising adamantane compounds which differed from the prior art compounds only in the presence of an ethylene rather than a methylene link in the structure; Shetty also claimed a method of curbing appetite in animals by administering his compounds. The prior art compounds had been previously described as antiviral agents.

Because of structural considerations, the C.C.P.A. held that Shetty needed to show an actual difference in properties between his compounds and those of the art; since he did not do this, the Court held the composition claim to be unpatentably obvious. Regarding the method claims, however, the Court held that the issue was whether the claimed method of curbing appetite would have been obvious. The fact that appellants' amount effective to curb appetite corresponded to the art's amount to combat microbial infestation or that both methods used oral administration did not persuade the C.C.P.A. that the claimed method

was obvious. Quoting its earlier decision in In re Naylor, 152 U.S.P.Q. 106, 108, the Court stated:

> [Inherency] is quite immaterial if, as the record establishes here, one of ordinary skill in the art would not appreciate or recognize that inherent result.

The Court went on to state:

> . . . The mere hindsight asserting that corresponding dosages render appellant's method obvious is untenable. Prior to appellant's disclosure, none of the adamantane compounds in any of the references before us suggested a use, much less a dosage, for curbing appetite.

Still further, it is well-known that new uses of old compounds can be patentable subject matter. The test of patentability for a method directed to a new use of an old compound is not whether the compound or composition inherently has properties which lead to the new use. The test is the unobviousness of the new use, In re Sebek et al, 146 U.S.P.Q. 44. If the process has an unobvious result and the particular use of the material is not suggested by the prior art, then the process is patentable; Ex parte Wagner, 88 U.S.P.Q. 217.

In view of the foregoing, it is believed that new Claims 22-92 are patentable as here presented. Further favorable action in the form of a Notice of Allowance is believed to be in order and is earnestly solicited.

If any issues remain unresolved which could be addressed in a telephone discussion, the Examiner is requested to telephone the undersigned at the number given below.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: Mary Katherine Baumeister
Mary Katherine Baumeister
Registration No. 26,254

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: March 18, 2003